

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference UTBA021PEP	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US00/02051	International filing date (day/month/year) 25/01/2000	Priority date (day/month/year) 25/01/1999
International Patent Classification (IPC) or national classification and IPC C12Q1/68		
Applicant UT-BATTELLE, LLC et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.


2. This REPORT consists of a total of 8 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☐ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☒ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 22/08/2000	Date of completion of this report 03.05.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Barz, W Telephone No. +49 89 2399 7320



**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US00/02051

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1-88 as originally filed

Claims, No.:

1-41 as originally filed

Drawings, sheets:

1/10-10/10 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

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☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☒ the entire international application.

☐ claims Nos. .

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
see separate sheet

☒ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

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2. Non-written disclosures (Rule 70.9)

see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

ITEM III:

1. For the following reasons, **claim 1** of the present application is not sufficiently supported by the description as required by Article 6 PCT:

Several features of claim 1 ("plurality of sources of electromagnetic radiation", "second detector", "second sensing element") are not mentioned in the description. Therefore, the nature of the present invention is not clear from the wording of claim 1.

While claim 1 relates to an integrated circuit comprising "a plurality of sources of electromagnetic radiation", it appears from the description that the present invention refers to a biochip comprising a single light source (page 5, line 13; page 11, lines 1-5; figures 1A-1C). In view of this fundamental difference between the claims and the description, the nature of the invention remains unclear after reading of the entire application. Consequently, claim 1 does not fulfill the requirement of Article 6 PCT that the claims must be supported by the description.

2. Furthermore, **claim 1** is unclear in the sense of Article 6 PCT, because it is not apparent how a circuit comprising "a plurality of sources of electromagnetic radiation", two detectors, two sensing elements and means for generating an output signal could be "capable of detecting two or more different target biomolecules". Thus, claim 1 is too unclear to allow a skilled person to perform the present invention, especially in the light of its lack of support in the description.
3. The dependent **claims 12, 14, 16, 23-24, and 32-33** contain several features (e.g. "light emitting diode", "laser array", "avalanche photodiode", "microprocessor", "chromogenic substrate", "green fluorescent protein etc.", "2x2, 6x6, 8x8 array of sensors") which are also not supported by the description, in contrast to the requirement of Article 6 PCT.
4. Finally, the description also does not seem to support the independent **claims 36-41**, because it appears to mention neither an apparatus, detection system, or detection kit comprising the circuit of claim 1, nor the use of said circuit, nor methods comprising the contacting of a sample with said circuit.

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5. In view of the above, the present patent application is not sufficiently supported by the description and is too unclear to allow examination of the present application (Article 34(4)(a)(ii) PCT).

ITEM VI:

Certain published documents (Rule 70.10)

Application No Patent No	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
WO 99/27140	3 June 1999	25 Nov. 1998	26 Nov. 1997

The above patent document was published after the priority date, but before the filing date of the present application. Therefore, it may become relevant prior art in the Regional phase of the present application.

ITEM VII:

1. The references on page 1, line 7, page 2, lines 21-22, page 8, line 28, and page 79, lines 6-7, refer to unpublished documents, in contrast to the requirement of PCT Guidelines II-4.18 that only published documents should be referred to.
2. The incorporation of disclosures by reference (see the passages on page 1, lines 6-8, page 2, line 23-24, page 8, line 28, page 17, line 28, page 21, line 27, page 22, lines 5, 11, 15, 23, and 35, page 23, lines 10 and 24, page 28, lines 17 and 32, page 45, lines 14-15, page 46, line 19, page 48, line 25, and page 79, lines 3-4) is not allowed (PCT Guidelines II-4.17).
3. Vague and not precisely defined expressions related to the "spirit" of the invention (page 48, line 35 and on page 88, lines 6 and 10) are unallowable (PCT Guidelines III-4.3a).

4. Finally, the vague and imprecise statement in the description on page 88, lines 7-11, implies that the subject-matter for which protection is sought may be different to that defined by the claims, thereby resulting in lack of clarity (Article 6 PCT) when used to interpret them (PCT Guidelines III-4.3a).

ITEM VIII:

1. It is clear from the description (e.g. on page 3, lines 22-34; page 4, line 24 - page 5, line 3; page 5, lines 15-24; figures 1A-1C and 4) that the present invention relates to the simultaneous detection of two or more different types of molecules (e.g. DNA and antigens) on a single biochip.

Since independent **claim 1** does not contain this feature, it does not meet the requirement following from Article 6 PCT taken in combination with Rule 6.3(b) PCT that any independent claim must contain all the technical features essential to the definition of the invention.

2. The term "operably associated" used in **claim 1**, steps (d) and (e) is unclear and leaves the reader in doubt as to the kind of association to which it refers, thereby rendering the definition of the subject-matter of said claim unclear (Article 6 PCT).
3. **Claims 19, 21, and 33** are unclear in the sense of Article 6 PCT, because they refer to the "plurality of probes" or "probes" of claim 1, although claim 1 does not mention any probes .
4. Similarly, **claim 24** is not clear (Article 6 PCT), because it refers to the "enzyme" of claim 3, although claim 3 does not mention any enzyme.
5. **Claim 26** is unclear in the sense of Article 6 PCT, because "X-ray", "microwave", "visible light, ultraviolet light, infrared light, near-infrared or near-ultraviolet light" are no "sources of electromagnetic radiation".
6. **Claim 28** is not clear (Article 6 PCT), because it refers to "said sensing elements" of claim 36, although claim 36 does not mention any such elements.

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International application No. PCT/US00/02051

7. Similarly, **claims 31 and 32** are unclear in the sense of Article 6 PCT, because they refer to the "plurality of sensors" of claim 1, although claim 1 does not mention any plurality of sensors.
8. It appears that **claim 35** should be dependent on claim 8 (instead of claim 2), because it includes all the features of claim 8.
9. Finally, **claim 40** is unclear (Article 6 PCT), because claim 1 does not mention "two or more of said sensors".

PATENT COOPERATION TREATY

PCT

09/890047

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER ACTION		see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
International application No.	International filing date (day/month/year)	(Earliest) Priority Date (day/month/year)	
PCT/US 00/ 02051	25/01/2000	25/01/1999	
Applicant			
LOCKHEED MARTIN ENERGY RESEARCH CORPORATION et al.			

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

MULTIFUNCTIONAL AND MULTISPECTRAL BIOSENSOR DEVICES AND METHODS OF USE

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☒ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

1A

☐ None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/IS 00/02051

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, PAJ, WPI Data, INSPEC, COMPENDEX, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	<p>WO 99 27140 A (LOCKHEED MARTIN) 3 June 1999 (1999-06-03) abstract page 25, line 7 - line 12 page 43, line 25 -page 51, line 10 page 78, line 12 -page 79, line 3 claims; figures 3-14 --- -/--</p>	1-41



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

24 July 2000

Date of mailing of the international search report

28/07/2000

Name and mailing address of the ISA

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Fax: (+31-70) 340-3016

Authorized officer

Thomas, R.M.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/S 00/02051

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>WO 93 22678 A (MIT) 11 November 1993 (1993-11-11)</p> <p>abstract page 1, paragraph 1 page 4, line 26 -page 5, line 5 page 7, line 27 -page 8, line 3 page 8, line 14 - line 24 page 9, line 4 - line 10 page 19, line 9 - line 21 page 24, line 8 - line 13 page 40, line 16 - line 21 page 41, line 19 -page 42, line 14 page 45, line 18 - line 21 table III</p>	<p>1-11, 13-17, 19-21, 27-37, 39-41</p>
A	<p>US 5 658 732 A (EBERSOLE) 19 August 1997 (1997-08-19) abstract column 1, line 18 - line 23 column 1, line 31 - line 34 column 6, line 24 - line 27 column 9, line 46 - line 52 column 14, line 33 - line 35</p>	<p>1</p>

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/02051

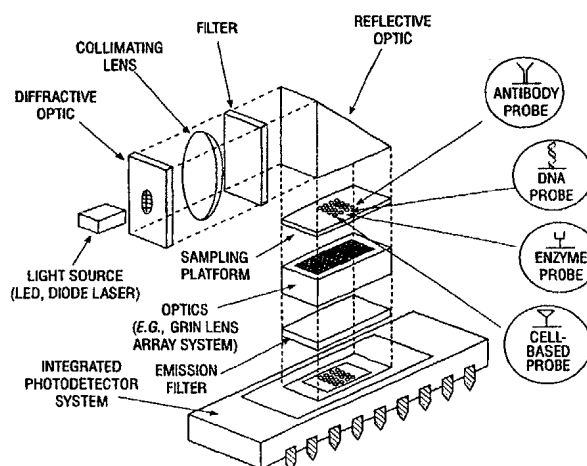
Patent document cited in search report		Publication date		Patent family member(s)		Publication date
WO 9927140	A	03-06-1999	AU	1609399 A		15-06-1999
WO 9322678	A	11-11-1993	US	5846708 A		08-12-1998
			EP	0638173 A		15-02-1995
			JP	7508831 T		28-09-1995
			US	5653939 A		05-08-1997
US 5658732	A	19-08-1997	CA	2066643 A		05-04-1991
			DE	69010506 D		11-08-1994
			DE	69010506 T		22-12-1994
			EP	0494896 A		22-07-1992
			JP	5500715 T		12-02-1993
			WO	9105261 A		18-04-1991



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁷ : C12Q 1/68	A3	(11) International Publication Number: WO 00/43552 (43) International Publication Date: 27 July 2000 (27.07.00)
(21) International Application Number: PCT/US00/02051 (22) International Filing Date: 25 January 2000 (25.01.00) (30) Priority Data: 09/236,758 25 January 1999 (25.01.99) US (71) Applicant (for all designated States except US): LOCKHEED MARTIN ENERGY RESEARCH CORPORATION [US/US]; Oak Ridge National Laboratory, P.O. Box 2009, Oak Ridge, TN 37831 (US). (72) Inventor; and (75) Inventor/Applicant (for US only): VO-DINH, Tuan [US/US]; Oak Ridge National Laboratory, 701 Scarboro Road, P.O. Box 20080 - MS 6101, Oak Ridge, TN 37831 (US). (74) Agent: MOORE, Mark, D.; Williams, Morgan & Amerson, P.C., Suite 250, 7676 Hillmont, Houston, TX 77040 (US).		(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i> (88) Date of publication of the international search report: 2 November 2000 (02.11.00)

(54) Title: MULTIFUNCTIONAL AND MULTISPECTRAL BIOSENSOR DEVICES AND METHODS OF USE

**(57) Abstract**

Disclosed are advanced multifunctional biochip devices capable of specifically detecting and quantitating multiple biomolecular target compounds, such as polypeptides, polynucleotides, and other intracellular and extracellular biomolecules. In illustrative embodiments, the miniaturized multifunctional biosensor device comprises multiple biological sensing elements, excitation micro-lasers, a sampling waveguide equipped with optical fluorescence detectors, integrated electro-optics, a bio-telemetric radio frequency signal generator, and a plurality of molecular probes, all contained on a single integrated circuit, or "biochip". The biochip is suitable for multi-gene analysis, and multi-peptide detection, as well as simultaneous detection and quantitation of polynucleotide and polypeptide species using a single biochip device. Also disclosed are methods that permit rapid, large-scale, and cost-effective production of such biochip devices, as well as their use in the detection and quantitation of multiple species in a single mixed biological sample.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

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INTERNATIONAL SEARCH REPORT

Inter Application No
PCT/US 00/02051

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

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C. DOCUMENTS CONSIDERED TO BE RELEVANT

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Date of the actual completion of the international search

24 July 2000

Date of mailing of the international search report

28/07/2000

Name and mailing address of the ISA

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Fax: (+31-70) 340-3016

Authorized officer

Thomas, R.M.

INTERNATIONAL SEARCH REPORT

Inter Application No
PCT/US 90/02051

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>W0 93 22678 A (MIT) 11 November 1993 (1993-11-11)</p> <p>abstract page 1, paragraph 1 page 4, line 26 -page 5, line 5 page 7, line 27 -page 8, line 3 page 8, line 14 - line 24 page 9, line 4 - line 10 page 19, line 9 - line 21 page 24, line 8 - line 13 page 40, line 16 - line 21 page 41, line 19 -page 42, line 14 page 45, line 18 - line 21 table III</p>	<p>1-11, 13-17, 19-21, 27-37, 39-41</p>
A	<p>US 5 658 732 A (EBERSOLE) 19 August 1997 (1997-08-19) abstract column 1, line 18 - line 23 column 1, line 31 - line 34 column 6, line 24 - line 27 column 9, line 46 - line 52 column 14, line 33 - line 35</p>	<p>1</p>

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 90/02051

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9927140	A	03-06-1999	AU 1609399 A	15-06-1999
WO 9322678	A	11-11-1993	US 5846708 A	08-12-1998
			EP 0638173 A	15-02-1995
			JP 7508831 T	28-09-1995
			US 5653939 A	05-08-1997
US 5658732	A	19-08-1997	CA 2066643 A	05-04-1991
			DE 69010506 D	11-08-1994
			DE 69010506 T	22-12-1994
			EP 0494896 A	22-07-1992
			JP 5500715 T	12-02-1993
			WO 9105261 A	18-04-1991